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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
07/565,673	08/10/90	VAN DER LAAN	J

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EXAMINER

FRONDA, C

ART UNIT	PAPER NUMBER
1652	<i>64</i>

DATE MAILED: 10/23/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

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Office Action Summary	Application No. 07/565,673	Applicant(s) Van Der Lann et al.
	Examiner Christian L. Fronda	Art Unit 1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on _____
 2a) This action is FINAL. 2b) This action is non-final.
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 41-55 is/are pending in the application.
 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
 5) Claim(s) _____ is/are allowed.
 6) Claim(s) 41-55 is/are rejected.
 7) Claim(s) _____ is/are objected to.
 8) Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
 10) The drawing(s) filed on _____ is/are objected to by the Examiner.
 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved.
 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
 a) All b) Some* c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

- 14) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) Notice of References Cited (PTO-892) 18) Interview Summary (PTO-413) Paper No(s). _____
 16) Notice of Draftsperson's Patent Drawing Review (PTO-948) 19) Notice of Informal Patent Application (PTO-152)
 17) Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ 20) Other: _____

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DETAILED ACTION

1. In the AMENDMENT dated July 24, 2001 (paper no.63), Applicants have amended claims 41, 45, 47, 48, and 50 and added new claims 54 and 55.
2. Claims 41-55 are under consideration in this Office Action.

Claim Rejections - 35 U.S.C. § 112, 1st Paragraph

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
4. Claims 41-53 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Because Applicants have not responded to this rejection, the claims stand rejected for the reasons stated in the Office Action dated March 29, 2001 (paper no. 61).

5. Claims 54 and 55 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed toward a gene encoding all possible "mutant high alkaline" proteases, all possible "derivatives" of *Bacillus novo* species PB92, all host *Bacillus* host cells incapable of producing a "wild-type high alkaline" proteases. The specification, however, only provides the following representative species of mutant alkaline proteases encompassed by these claims: gene encoding a mutant alkaline protease comprising a nucleotide sequence consisting of the gene encoding the wild-type alkaline protease of *Bacillus novo* species PB92 having the codon for M216 replaced with a codon coding for Q, the codon for S160 replaced with a codon coding for D, or the codon of N212 replaced with a codon coding for D. The specification only teaches the wild-type alkaline protease of *Bacillus novo* species PB92 as the single representative

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species of the claimed "wild-type high alkaline" proteases. The specification only discloses *Bacillus novo* species PB92 as the *Bacillus* host. There is no disclosure of any particular structure to function/activity relationship in the disclosed species of the wild-type protease of *Bacillus novo* species PB92 or the gene encoding the wild-type alkaline protease of *Bacillus novo* species PB92 having the codon for M216 replaced with a codon coding for Q, the codon for S160 replaced with a codon coding for D, or the codon of N212 replaced with a codon coding for D. Furthermore, there is no written description of any "derivative" of *Bacillus novo* species PB92.

The specification also fails to describe additional representative species of these "mutant high alkaline" proteases, "wild-type high alkaline" proteases, and "derivatives" of *Bacillus novo* species PB92 by any identifying structural characteristics or properties for which no predictability of structure is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

6. Claims 41-55 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the wild-type alkaline protease of *Bacillus novo* species PB92, the gene encoding said wild-type alkaline protease of *Bacillus novo* species PB92, and a gene encoding a mutant alkaline protease comprising a nucleotide sequence consisting of the gene encoding the wild-type alkaline protease of *Bacillus novo* species PB92 having the codon for M216 replaced with a codon coding for Q, the codon for S160 replaced with a codon coding for D, or the codon of N212 replaced with a codon coding for D; does not reasonably provide enablement for any wild-type alkaline protease or any gene encoding any mutant alkaline protease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicants' arguments filed July 24, 2001 (paper no.63) have been fully considered but they are not persuasive. Applicants argue that the specification is enabling for the instant claims and that a "variety of high alkaline proteases were known by those of skill in the art".

The nature and breadth of the claims encompass any wild-type alkaline proteases or any genes encoding any mutant alkaline proteases. However, the specification provides guidance and examples for the wild-type alkaline protease of *Bacillus novo* species PB92 and a gene encoding a mutant alkaline protease comprising a nucleotide sequence consisting of the gene encoding the wild-type alkaline protease of *Bacillus novo* species PB92 having the codon for M216 replaced with a codon coding for Q, the codon for S160 replaced with a codon coding for D, or the codon of N212 replaced with a codon coding for D. Knowledge regarding the specific source and type of wild-type alkaline protease and the specific mutation in the claimed gene encoding the mutant alkaline protease is lacking. Thus, searching for the specific wild-type alkaline protease and the

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specific mutation in the claimed gene encoding the mutant alkaline protease is well outside the realm of routine experimentation and predictability in the art of success is extremely low. The amount of experimentation to practice the claimed invention is enormous and entails screening a vast number of organisms for an organism containing a wild-type alkaline protease, selecting and isolating a wild-type alkaline protease from the selected biological source, obtaining the amino acid sequence of the isolated wild-type alkaline protease, obtaining the gene encoding the isolated wild-type alkaline protease from libraries constructed from the selected biological source, and recombinantly expressing the wild-type protease using the gene encoding the wild-type protease. Furthermore, such experimentation entails selecting a wild-type alkaline protease to mutate, selecting a mutation to perform on the amino acid sequence of the wild-type alkaline protease such as substitution, addition, deletion, or combinations thereof of amino acid residues, obtaining the gene encoding the selected wild-type alkaline protease, mutate the gene encoding the wild-type alkaline protease, express the mutant alkaline protease, and screening for mutants that still have alkaline protease activity.

In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

Claim Rejections - 35 U.S.C. § 112, 2nd Paragraph

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
8. Claims 41, 42-47, 54, and 55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 41 is indefinite because it is not known what specific amino acid residue(s) in the claimed "mutant high alkaline protease" are to be mutated and one of skill in the art cannot determine the metes and bounds of the claimed invention. Claims 42-47 which depend from claim 41 are also rejected because they do not correct the defect of claim 41.

In claim 54, the phrases "Bacillus novo species PB92 and its derivatives" and "Bacillus novo species PB92 or derivative thereof" renders the claim indefinite because the specific "derivatives" of the claimed "Bacillus novo species PB92" are not known and defined in the specification and one of skill in the art cannot determine the metes and bounds of the claimed

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invention. Claim 55 which depends from claim 54 are also rejected because the claim does not correct the defect of claim 54.

Conclusion

9. No claim is allowed.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Claims drawn to a method for producing a mutant alkaline protease comprising expressing in a mutant alkalophilic *Bacillus* host, a mutant alkaline protease encoded by a polynucleotide comprising a nucleotide sequence which has the codon for M216, S160, or N212 of the gene encoding the wild-type alkaline protease of *Bacillus* novo species PB92 replaced with another codon encoding another amino acid, wherein said mutant alkalophilic *Bacillus* host comprises a chromosomal deletion of the gene encoding the wild-type alkaline protease of *Bacillus* novo species PB92, may overcome the stated rejections.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L. Fronda whose telephone number is (703)305-1252. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703)308-3804. The fax phone number for this Group is (703)308-0294. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703)308-0196.

CLF


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